An oscillatory expression of the bHLH TF Asense sequentially regulates the specification of neurogenic progenitors and cell cycle exit of neuronal precursors in the Drosophila larval brain

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During Brain development there are two key steps that must be tightly regulated: The switch from proliferating (symmetrically dividing) to neurogenic (asymmetrically dividing) neural progenitors, and the regulation of terminal differentiation of the precursor cells. The Drosphila larval optic lobe (OL) provides a suitable experimental model in which to study the genetic basis underlying those processes during neurodevelopment. Thus, OL neuroepithelial (NE, proliferating progenitors) cells differentiate into Neuroblasts (NB, neurogenic progenitors). This transition occurs synchronously in a row of cells performing a proneural wave. The synchrony and the order of this process make the OL a perfect model to better understand the regulation of this key transition. Those NBs, in turn, give rise to lamina precursor cells and medulla neurons.

The *achaete-scute* gene complex (*AS-C*) encodes TFs of the bHLH family required for the formation of neural precursors. It has been described that the NE-NB transition is triggered by the expression of *lethal of scute (l'sc,* an *AS-C* gene). This expression depends on the integration of EGFR, Notch and JAK/STAT signaling pathways.

Our lab has found that a transitory expression of *asense* (*ase,* another *AS-C* gene) is necessary for the terminal differentiation of medulla neurons inducing the cell cycle exit through the regulation of the cyclin-depend kinase, *dacapo (dap).* Interestingly, we have observed that *ase* is also transiently upregulated in the transition from NE to NB. Given the known proneural function of the mammalian *ase* orthologue Ascl1/Mash1, we have analyze the possible functions of Ase in the regulation of the OL proneural wave. We have examined the consequences of this transitory expression as well as its role of the regulation of the cell cycle in this process. We found that Ase is required for a correct NE-NB transition and, moreover, is sufficient to induce this transition in a L'sc non-mediated manner. Hence, we describe here by first time a proneural role of Ase in the CNS. Together, our data suggest that the oscillatory expression of Ase along the sequential step of neurogenesis is a crucial mechanism for the transcriptional control of the proliferation/differentiation balance during brain development in *Drosophila.*

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